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Abstract: Transcatheter aortic root repair (TARR) is still not available because of the complex anatomy. In order to develop future TARR technologies, a human-derived bench test model is required before performing animal tests. For this purpose, we aimed to validate computed tomography (CT)-derived 3D-printed root models for TARR technologies. Four human CT-derived roots were printed using different resins: Visijet M3 Crystal, Photopolymer gel SUP705, Formlabs flexible resin, and Materialise HeartPrint Flex. A stress test was performed using a 26-mm balloon-expandable Sapien valve deployed in aortic position. The too rigid Visijet M3 Crystal was not tested. Among the others, all but one (HeartPrint Flex) ruptured during the test showing low wall resistances. Further tests were then performed in two roots made of HeartPrint Flex resin. The anatomic validation was performed comparing human CT scan-derived 3D reconstructions and CT scan measurements: a mean difference of 0.57 ± 0.4 mm for aortic annulus diameter and for the distance between the aortic annulus and the coronary ostia was measured. Concerning the coronary arteries, they are of paramount importance for new TARR technologies, and therefore, we tested the coronary flows of the HeartPrint Flex root at different pressure levels. At 60 mm Hg, right and left mean adjusted coronary flows were 471 and 663 ml/min; at 80 mm Hg, right and left mean coronary flows were 551 and 777 ml/min; and at 100 mm Hg, right and left mean coronary flows were 625 and 858 ml/min. In our study, 3D-printed root models correlate well with human anatomy and guarantee physiologic coronary flows for TARR technologies.

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Suitability of 3D-Printed Root Models for the Development of Transcatheter Aortic Root Repair Technologies

Enrico Ferrari,* Giulia Piazza,† Martin Scoglio,† Denis Berdajs,‡ Piergiorgio Tozzi,† Francesco Maisano,§ and Ludwig Karl Von Segesser†

Transcatheter aortic root repair (TARR) is still not available because of the complex anatomy. In order to develop future TARR technologies, a human-derived bench test model is required before performing animal tests. For this purpose, we aimed to validate computed tomography (CT)-derived 3D-printed root models for TARR technologies. Four human CT-derived roots were printed using different resins: Visijet M3 Crystal, Photopolymer gel SUP705, Formlabs flexible resin, and Materialise HeartPrint Flex. A stress test was performed using a 26-mm balloon-expandable Sapien valve deployed in aortic position. The too rigid Visijet M3 Crystal was not tested. Among the others, all but one (HeartPrint Flex) ruptured during the test showing low wall resistances. Further tests were then performed in two roots made of HeartPrint Flex resin. The anatomic validation was performed comparing human CT scan-derived 3D reconstructions and CT scan measurements: a mean difference of 0.57 ± 0.4 mm for aortic annulus diameter and for the distance between the aortic annulus and the coronary ostia was measured. Concerning the coronary arteries, they are of paramount importance for new TARR technologies, and therefore, we tested the coronary flows of the HeartPrint Flex root at different pressure levels. At 60 mm Hg, right and left mean adjusted coronary flows were 471 and 663 ml/min; at 80 mm Hg, right and left mean coronary flows were 551 and 777 ml/min; and at 100 mm Hg, right and left mean coronary flows were 625 and 858 ml/min. In our study, 3D-printed root models correlate well with human anatomy and guarantee physiologic coronary flows for TARR technologies. *ASAIO Journal* XXX; XX:00–00.

Key Words: transcatheter aortic root replacement, 3D printing, aortic valve disease, aortic root disease.

Despite surgical aortic valve replacement remains the treatment of choice for symptomatic aortic valve disease, the transcatheter aortic valve replacement (TAVR) has become a valid alternative in selected high-risk patients.[1–8] Conversely, because of the complex anatomy, the aortic root disease, combined or not with a valve dysfunction, is still not addressed with transcatheter techniques and patients at high risk for surgery can only undergo TAVR without root replacement or standard surgical procedures requiring cardiopulmonary bypass, root replacement, and coronary reimplantation.

Studies in the field of transcatheter aortic root replacement (TARR) are at their earlier phase, and, therefore, bench test models based on human anatomy will be of paramount importance before animal experimentation.[9] Three-dimensional printing is becoming popular in medicine, and, therefore, human computed tomography (CT) scan-derived 3D-printed root models can be employed to develop new technologies for TARR.[10–12] However, aortic roots are anatomically complex, and 3D models should not only guarantee enough resistance during the implantation of expandable endografts but also patent coronary artery ostia to test intracoronary flows after the device implantation. In this preliminary study, we prototyped 3D-printed root models with patent coronary ostia derived from human CT scan by using different available 3D printers and resins. Then, we validated the anatomic model, we tested the resistance during the implantation of a balloon-expandable transcatheter device, and we performed hydrodynamic tests to verify the coronary flow.

Methods

Three-Dimensional Prototyping

Computed tomography scan images of patients treated with TAVR using 26-mm Sapien valves (Edwards Lifesciences, Irvine, CA) and presenting with a smoothly dilated ascending aorta were used for this study. Informed consent for data analysis was provided. Gated CT scan images taken at midsystole were imported and analyzed with Mimics 18.0 software by Materialise (Louvain, Belgium), an anatomic modeling software. The blood inside the ascending aorta (up to 10 cm above the aortic valve annulus) and the root (the left ventricle outflow tract, 2 cm below to the aortic valve annulus) was isolated to extract the inner surface. A thickness of 2 mm was added to the model in order to reproduce standard aortic wall thickness (**Figure 1**, A–C). Anatomic calcifications of the aortic valve leaflets were electronically added to the models during CT scan modeling by following the natural borders. Considering the twofold purpose of the study consisting in both creating and validating 3D-printed root models for TARR technologies, and also confirming the presence of coronary flows after the implantation of endovascular devices, we decided to focus on 3D coronary artery anatomy without creating complex (and more expensive) root models with two physical characteristics, one for the aortic wall and one for the aortic valve.[11] Concerning the coronary arteries take-offs, their internal diameter was slightly

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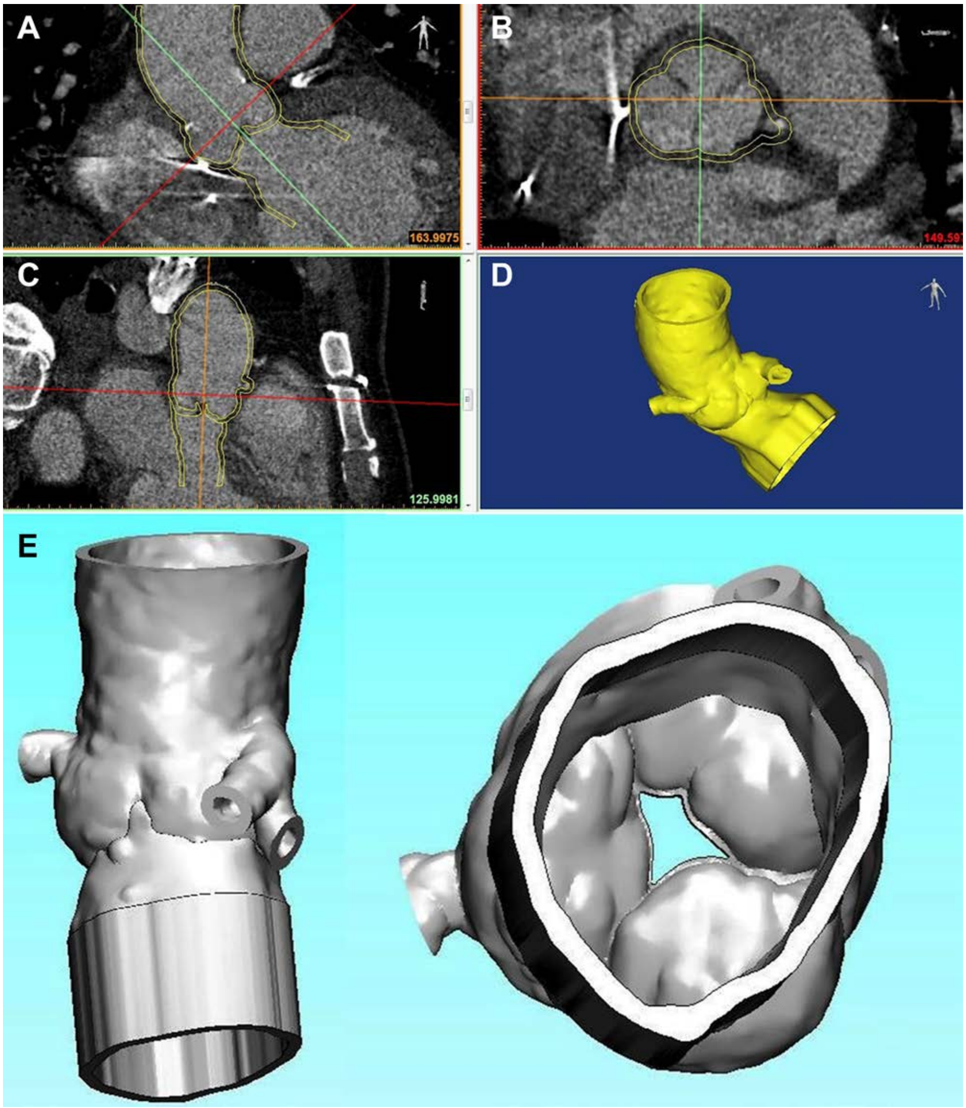

Figure 1. A–C: Computed tomography scan segmentation with Mimics 18.0 software (Materialise): 1 cm of thickness was added to the inner surface of the aortic root after having isolated the blood. This thickness represents the aortic root wall and the valve leaflets; (**D**) 3D prototyping using the Mimics 18.0 software (Materialise); (**E**) 3D reconstruction with the 3-Matic 10.0 modeling software (Mimics Innovation Suite) employed to obtain the final models for 3D printing.

increased during computed anatomic modeling because of the difficulty of 3D printing, with the available technology, little vessels with small inner diameters.

Three-dimensional models were then engineered using the Mimics 18.0 software that generated semiautomatic segmentation of CT scan images (**Figure 1D)**. The 3-Matic 10.0 modeling software (Mimics Innovation Suite) was finally used to obtain 3D reconstructions for printers (**Figure 1E)**, and data were sent to different providers who printed root models with different resins.

Validation Test

To confirm that 3D-printed root models replicate CT-derived human anatomy and dimensions, we compared measurements made on 3D reconstructions (with Netfabb software) with those made on corresponding original CT scan images. The coronary inner diameter, the aortic annulus diameter, and the distance between the aortic annulus and the coronary ostia were measured (**Figure 2**). Each measurement was performed two times.

Stress Test

Four 3D-printed root models made of 4 different resins were stressed with the deployment of balloon-expandable 26 mm transcatheter valves within the aortic annulus. The root models damaged during the implantation were discarded and not used for further tests.

Coronary Test

In order to use 3D-printed roots for TARR technology development, coronary flows in the 3D model should be as similar as possible to human coronary flows. Therefore, the flow through the coronary arteries of two 3D-printed root models that passed the stress test was measured at different diastolic pressure levels

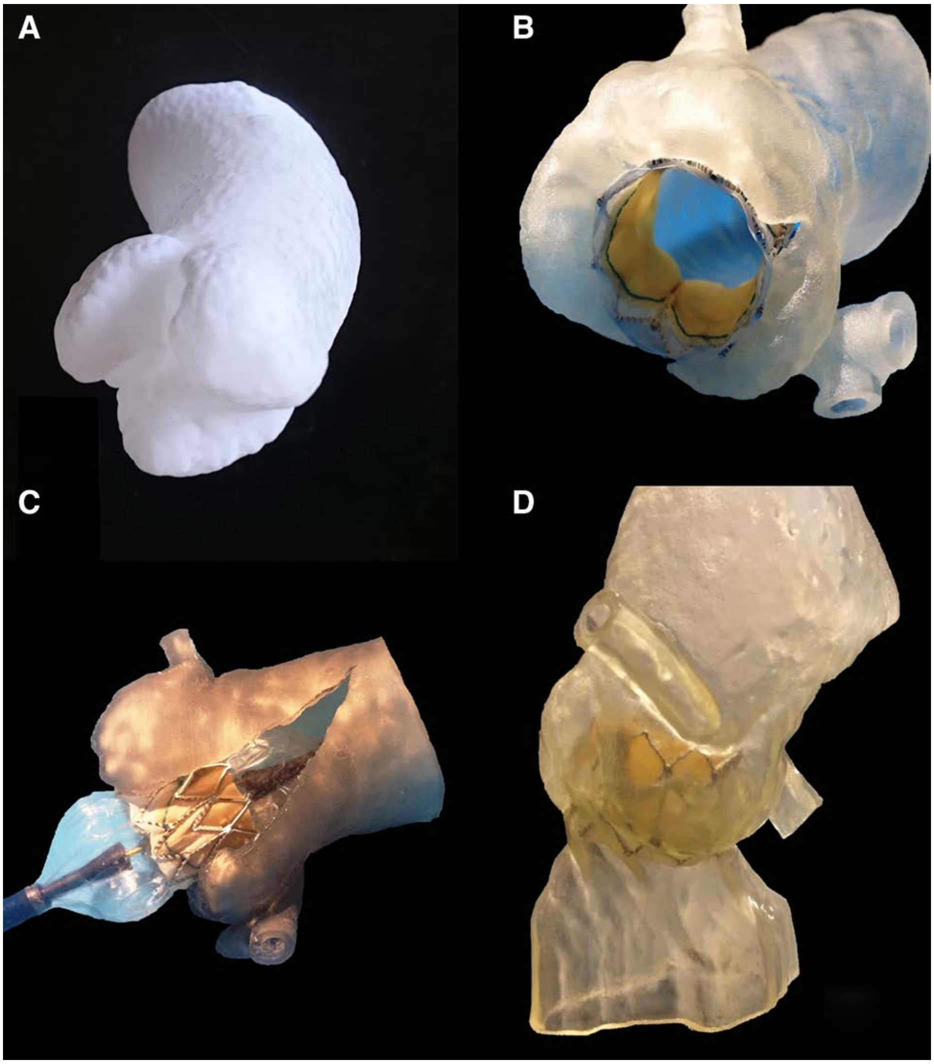

Figure 2. Three-dimensional-printed root models: (**A**) Visijet M3 Crystal (MJP) resin; (**B**) Photopolymer gel SUP705 resin with an implanted 26-mm Sapien valve; (**C**) Formlabs flexible resin with an implanted 26-mm Sapien; and (**D**) Materialise HeartPrint Flex resin with a 26-mm Sapien valve.

in a bench model. Data were compared with standard physiologic coronary flow rate which is 250 ml/min at rest for each coronary artery and can increase sixfold during exercise.[13,14] All measurements were performed in a nonpulsatile system without coronary resistances. The bench system was composed of silicon tubes and a reservoir from a standard cardiopulmonary bypass circuit. The inflow of the reservoir was connected to a source of water, whereas the outflow was connected to the ascending aorta of the root model (**Figure 3A)**. Small silicon tubes were also connected to the coronary arteries and placed into volumetric tanks to collect the water (**Figure 3B)**. The level of the reservoir was adjustable in order to obtain different heights and, therefore, different inflow pressures compatible with physiologic intra-aortic diastolic pressures: we tested the models at 81.6, 108.8, and 136 cm of water corresponding to 60, 80, and 100 mm Hg of pressure, respectively.

Left and right coronary flow rates were quantified by measuring the water accumulated in specific volumetric tanks connected to the coronary arteries (ml): each measurement was performed three times during a period of time of 10 seconds. Results were multiplied by six in order to obtain the quantity of water that can accumulate in the tank (in ml) during a period of time of 1 minute. As a result, a mean coronary flow value (ml/min) was obtained. Values were adjusted to overcome the limit of our system. First, adjustment was to consider only half coronary flow because our system was not pulsatile. Then, we considered two third of the value in order to obtain the equivalent of a human diastolic coronary flow (which is 2/3 of the total flow; only in diastole).

Statistical Analysis

Continuous variable is reported as means ± standard deviation.

Results

Validation Test

The accuracy of four 3D prototyped models was validated by measuring and comparing, both on CT scan images and computed 3D reconstructions, the sagittal and the coronal

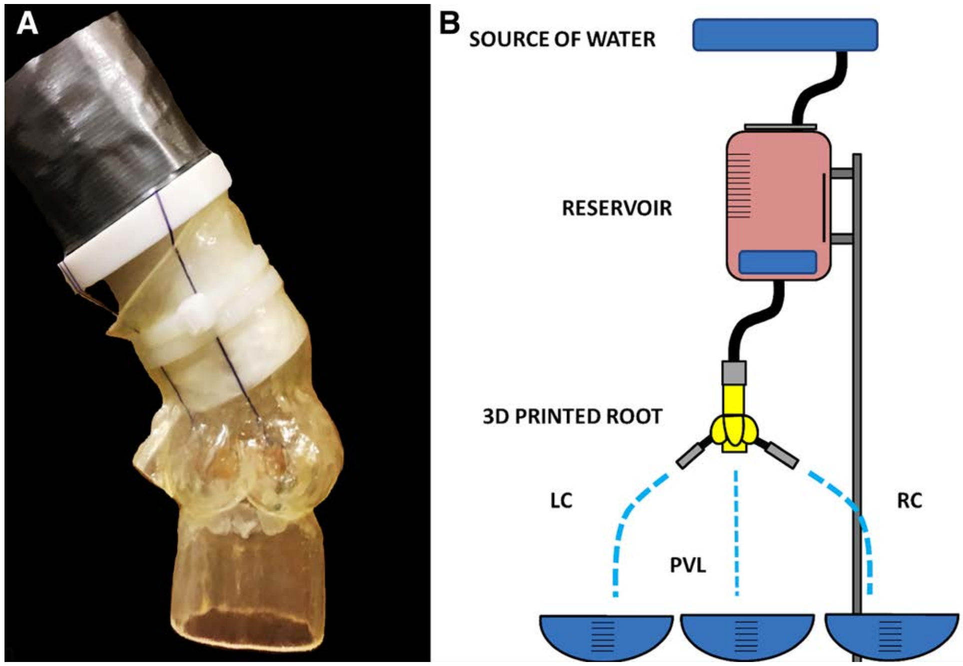

Figure 3. A: Three-dimensional-printed root model (HeartPrint Flex resin) with a 26-mm Sapien valve in aortic position; (**B**) Schema of the bench test: the 3D-printed root is connected to the reservoir, and the coronary arteries are connected to small tubes (8 mm diameter) draining into volumetric tanks. The level of the reservoir is adjustable for different diastolic pressure levels.

diameter of the aortic valve annulus, the distance between the aortic annulus and the coronary ostia, and the internal diameter of the coronary ostia (**Figure 4**). Measures are listed in **Table 1**. Aortic annulus diameters and annulus-to-coronary ostia distance measurements showed a mean difference of 0.57 ± 0.4 mm. To what may concern the values of the coronary inner diameters, they were expected higher in 3D reconstructions because of the 1.5–2 mm oversize that was necessarily added during the prototyping process in order to obtain patent 3D-printed coronary arteries. Therefore, there was a mean difference of 1.9 ± 0.3 mm.

Stress Test

Characteristics of four different tested resins are summarized in **Table 2**. The first root model (test 1) was made using the Projet 3510 SD printer (3D Systems, CA) that works with the Visijet M3 Crystal resin. This plastic has a high-stress resistance, but it is too rigid, not flexible at all, and does not allow the positioning of deployable transcatheter devices (**Figure 2A)**. Therefore, this root was not tested with the self-expandable valve.

Tests were performed using the Objet500 Connex 3 printer (Zedax SA, Switzerland) (test 2) and the Formlabs Form +1 printer (Formlabs, MA) (test 3). The main advantage of the Zedax printer was the possibility of changing the characteristics (flexibility) of the resin to get closer to the desired properties of the final aortic root model. With the Formlabs printer, the hardness of the resin cannot be changed and the only way to modify the flexibility of the printed model was to vary the thickness of the aortic wall (1.5–2.0 mm). Both 3D-printed root models were more flexible and elastic than the previous one, and we tested both by implanting an available transcatheter aortic device. A 26-mm Sapien valve was deployed within the two 3D-printed roots with nominal balloon inflation. The Zedax model showed a better resistance, but some tears appeared and were too large to be able to further test the functionality of the model (**Figure 2B)**. During the balloon inflation, the Formlabs model broke obliquely along the entire length of its lateral face, between the right and the left coronary ostia (**Figure 2C)**.

The fourth test (test 4) was performed with the Objet500 Connex 3 printer (Zedax SA, Switzerland) from Materialise which uses the HeartPrint Flex resin. A published compliance study showed a distensibility (D) of the HeartPrint Flex resin similar to the human arterial wall.[15] This root model was also tested with a 26-mm Sapien valve: during the deployment, the root model was not damaged, and the transcatheter valve properly adhered to the annulus (**Figure 2D)**.

Coronary Tests

We performed tests in two 3D-printed root models made of HeartPrint Flex resin with two deployed 26-mm balloon-expandable valves. The roots ware placed in the bench test system described above. Results of hydrodynamic tests are shown in **Table 3**. Because of missing coronary resistances, low liquid viscosity, and nonpulsatility, the total inflow rate (9.1 L/min) was twofold the normal human cardiac output (4–5 L/min). We divided the values by two, and we took two third of the results to compare with human diastolic coronary volumes. Modified results are listed in **Table 4**. In root 1, at 60 mm Hg of pressure, right and left mean coronary flow rates were 446 and 617 ml/min, respectively; at 80 mm Hg, coronary flow rates were 547 ml/min (right) and 750 ml/min (left); at 100 mm Hg, coronary flows were 607 ml/min (right) and 817 ml/min (left). In root 2, coronary flow results were similar to root 1 (**Table 3**). No valve blow-out was observed during the pressurized coronary tests.

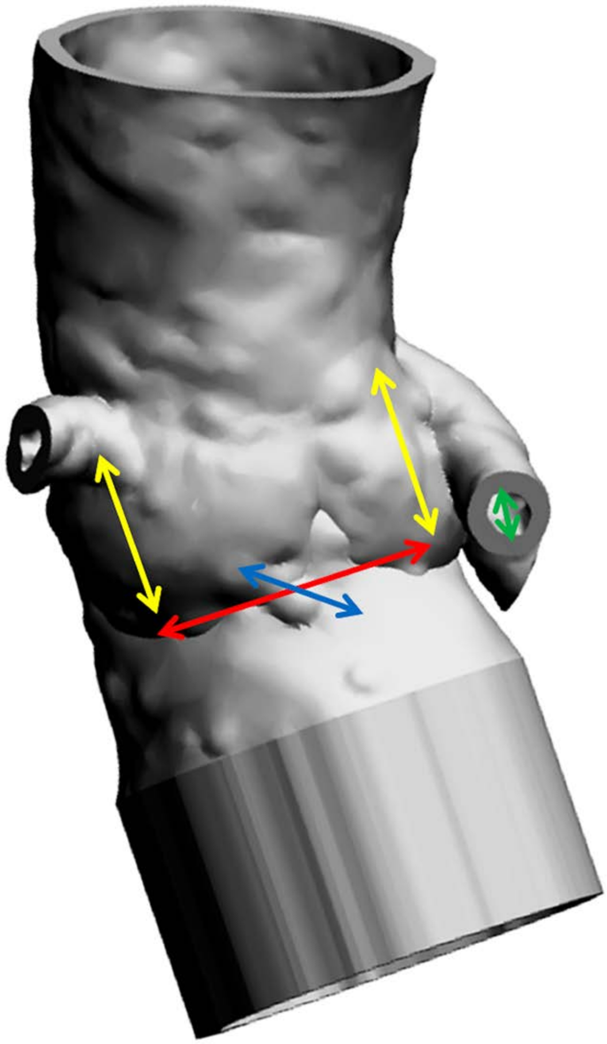

Figure 4. Three-dimensional-printed root models was validated by measuring and comparing, both on computed tomography (CT) scan images and 3D reconstructions, the sagittal and the coronal diameter of the aortic valve annulus (blue and red arrows), the distance between the aortic annulus and the coronary arteries (yellow arrows), and the diameter of the coronary ostia (green arrow).

Discussion

Three-dimensional printing is a helpful technology in many medical fields such as neurosurgery, maxillofacial surgery, and orthopedic surgery, and it is gaining popularity in pediatric and adult cardiovascular surgery for surgical planning and training.[16–22] We report our study on CT scan-derived root models that can be used during the development of innovative TARR technologies. Because the anatomy of the aortic root is complex, the models should guarantee adequate coronary diameters in order to allow the placement of coronary endografts or alternative solutions for coronary perfusion during TARR. Compared with other previously published studies that analyzed 3D-printed aortas for TAVR, we focused more on coronary artery patency by testing the flows in the printed roots with deployed transcatheter aortic valve devices.[10–12]

We first printed roots with characteristics similar to the human vascular tissue in order to deploy transcatheter devices without model damage. As already reported, the HeartPrint Flex resin shows similarities with aortic human tissues (elastic modulus [E1; 5%–25% stress] of 0.91 ± 00.2 MPa and maximal stress of 2.06 ± 0.23 MPa; D of $1.9–3.7 \times 10^{-3}$ mm Hg^{-1} [ascending aorta: $E = 1.24 \pm 0.563$ MPa and $D = 4.1 \pm 2.1 \times 10^{-3}$ mm Hg^{-1}]), and we successfully used this material for roots that passed the stress test.[15] However, diseased human aorta has heterogeneous characteristics that cannot be easily replicated with same accuracy, and valve leaflets do not have same physics structure as arteries.[23,24] Maragiannis *et al.*[11] used two different resins for the 3D-printing process of the valve and the aorta: the TangoPlus FLX930 is a rubber-like material with E1 of 0.146 MPa at 20% strain that they employed for printing the aortic wall. Nevertheless, the authors did not test the coronary artery patency. In another report, Ripley *et al.*[12] used the Formlabs clear flexible resin for the aorta (the same we used for test number 3) and 3D-printed Sapien valve phantoms made of a much more rigid resin.[10] They were able to insert the valves within the aortas, but the placement was not performed, as it happens in real life, with a balloon valve inflation. Also in this experiment, the coronary arteries were printed but not tested.

Therefore, because the aim of our study is to conceive a model for the TARR technology development, we created roots

Table 1. Anatomic Validation of Four 3D-Prototyped Aortic Root Models (Mean Values)

	CT Scan Images	Computed 3D Reconstructions	Difference in mm (%)
Root 1			
Sagittal aortic annulus diameter (mm)	26.3	26.3	0.0 (0%)
Coronal aortic annulus diameter (mm)	22.2	20.9	−1.3 (−5.8%)
Aortic annulus-right coronary ostium distance (mm)	13.3	13	−0.3 (−2.2%)
Aortic annulus-left coronary ostium distance (mm)	12	12.5	+0.5 (+4.1%)
Left coronary artery diameter (mm)	3.5	5*	+1.5 (+50%)
Right coronary artery diameter (mm)	2.8	4.5*	+1.7 (+60%)
Root 2			
Sagittal aortic annulus diameter (mm)	28.3	28.7	+0.4 (+1.4%)
Coronal aortic annulus diameter (mm)	26.9	26.3	−0.6 (−2.2%)
Aortic annulus-right coronary ostium distance (mm)	21.6	22.1	−0.5 (−2.3%)
Aortic annulus-left coronary ostium distance (mm)	17.1	16.1	−1.0 (−5.8%)
Left coronary artery diameter (mm)	3.3	5.3*	+2.0 (+60%)
Right coronary artery diameter (mm)	3.4	5.9*	+2.5 (+73%)

*2 mm added during prototyping.
CT, computed tomography.

Table 2. Characteristics of 3D Printers and Resins Employed to print Four 3D Root Models

	3D Printer (Company)	Plastic/Resin	Resistance	Rigidity	Flexibility
Test 1	Project 3510 SD (3D Systems, CA)	Visijet M3 Crystal (MJP) (translucent/biocompatible)	++++	++++	+
Test 2	Object 500 Connex3 (Zedax SA, Switzerland)	Photopolymer gel SUP705	++	+	++++
Test 3	Form +1 (Formlabs, MA)	Formlabs flexible resin	+	+	++++
Test 4 (root 1 and root 2)	Object 500 Connex 3 (Zedax SA, Switzerland)	Materialise HeartPrint Flex resin	+++	++	+++

Table 3. Coronary Test in Two 3D-Printed Root Models (HeartPrint Flex Resin)

	60 mm Hg	80 mm Hg	100 mm Hg
Root 1			
Left coronary artery flow (ml/min)	1,920/1,830/1,800 Mean: 1,850 ± 50.9 Diastolic flow: 1,233	2,280/2,250/2,220 Mean: 2,250 ± 24.5 Diastolic flow: 1,500	2,460/2,430/2,460 Mean: 2,450 ± 14.1 Diastolic flow: 1,633
Right coronary artery flow (ml/min)	1,350/1,350/1,310 Mean: 1,337 ± 18.9 Diastolic flow: 891	1,650/1,650/1,620 Mean: 1,640 ± 14.1 Diastolic flow: 1,093	1,800/1,800/1,860 Mean: 1,820 ± 28.3 Diastolic flow: 1,213
Paravalvular leak (ml/min)	1,380/1,350/1,380 Mean: 1,370 ± 14.1 Diastolic flow: 913	1,860/1,920/1,800 Mean: 1,860 ± 49.0 Diastolic flow: 1,240	2,340/2,490/2,310 Mean: 2,380 ± 78.7 Diastolic flow: 1,587
Root 2			
Left coronary artery flow (ml/min)	2,100/2,040/2,250 Mean: 2,130 ± 88.3 Diastolic flow: 1,420	2,460/2,400/2,400 Mean: 2,420 ± 28.3 Diastolic flow: 1,613	2,700/2,700/2,700 Mean: 2,700 ± 0 Diastolic flow: 1,800
Right coronary artery flow (ml/min)	1,500/1,470/1,500 Mean: 1,490 ± 14.1 Diastolic flow: 993	1,650/1,680/1,680 Mean: 1,670 ± 14.1 Diastolic flow: 1,113	1,920/1,920/1,950 Mean: 1,930 ± 14.1 Diastolic flow: 1,287
Paravalvular leak (ml/min)	1,800/1,740/1,680 Mean: 1,740 ± 49.0 Diastolic flow: 1,160	2,250/2,070/2,220 Mean: 2,180 ± 78.7 Diastolic flow: 1,453	3,060/2,850/2,760 Mean: 2,890 ± 125.7 Diastolic flow: 1,926

Table 4. Adjusted Coronary Test Results of Two 3D-Printed Root Models (HeartPrint Flex Resin)

	60 mm Hg	80 mm Hg	100 mm Hg
Root 1			
Left coronary artery flow (ml/min)	960/915/900 Mean: 925 Diastolic flow: 617	1,140/1,125/1,110 Mean: 1,125 Diastolic flow: 750	1,230/1,215/1,230 Mean: 1,225 Diastolic flow: 817
Right coronary artery flow (ml/min)	675/675/655 Mean: 668 Diastolic flow: 446	825/825/810 Mean: 820 Diastolic flow: 547	900/900/930 Mean: 910 Diastolic flow: 607
Paravalvular leak (ml/min)	690/675/690 Mean flow: 685 Diastolic flow: 457 At 80 bpm: 5.7 ml/beat	930/960/900 Mean flow: 930 Diastolic flow: 620 At 80 bpm: 7.7 ml/beat	1,170/1,245/1,155 Mean flow: 1,190 Diastolic flow: 793 At 80 bpm: 9.9 ml/beat
Root 2			
Left coronary artery flow (ml/min)	1,050/1,020/1,125 Mean: 1,065 Diastolic flow: 710	1,230/1,200/1,200 Mean: 1,210 Diastolic flow: 807	1,350/1,350/1,350 Mean: 1,350 Diastolic flow: 900
Right coronary artery flow (ml/min)	750/735/750 Mean: 745 Diastolic flow: 497	825/840/840 Mean: 835 Diastolic flow: 556	960/960/975 Mean: 965 Diastolic flow: 643
Paravalvular leak (ml/min)	900/870/840 Mean flow: 870 Diastolic flow: 580 At 80 bpm: 7.2 ml/beat	1,125/1,035/1,110 Mean flow: 1,090 Diastolic flow: 726 At 80 bpm: 9.1 ml/beat	1,530/1,425/1,380 Mean flow: 1,445 Diastolic flow: 963 At 80 bpm: 12 ml/beat

Two third of the half total flow.

with good coronary ostia instead of roots made of two different resins, one for the aorta and one, more resistant, for the valve. This brought two advantages: first, the production cost of 3D root models was lower, and second, the 3D prototyping and printing was simpler and faster.

To what may concern the anatomic validation, our results are compared with similar measurements made by Ripley *et al*.[12] in their study: the difference in minimum and maximum annulus diameter on 3D-printed models and corresponding CT scan images was less than half a millimeter. However, in their report, they did not measure coronary diameters and the distance between the coronary artery ostia and the aortic valve annulus. A limitation of 3D computed prototyping process is that some details cannot yet be reproduced in detail, and therefore, some approximation is required when printing small vessels such as the coronary arteries. In our experience, this approximation overcame the risk of printing aortic roots for TARR simulations with inadequate coronary arteries.

Once the roots were 3D printed, we implanted transcatheter valves to mimic the presence of one part of future TARR devices and we tested the coronary flows. It is conceivable that TARR devices will be composed of complex aortic endografts, valve prosthesis, valved endografts, and coronary endografts, and it is therefore very important that 3D printed roots for TARR simulation not only replicate human anatomy but also guarantee physiologic coronary flows during the tests. After adequate approximations given by the limits of the system, we demonstrated that the coronary flow in the models was comparable with human coronary flow. Nevertheless, in order to improve the precision of the measurements during the development of TARR technologies, tests should be performed in closed-loop hydrodynamic machines using pulsatile anterograde flow, physiologic volume, coronary resistances, and liquids with physiologic viscosity. Moreover, future models could also be "bio-printed" using new technologies that employ biocompatible materials.[25,26] In conclusion, 3D printing is more accessible and less expensive (in our experience: €450 per root) than years ago, and its applications have increased in the field of surgical planning, education, teaching, and simulation. Computed tomography-derived 3D-printed root models from diseased human anatomies (bicuspid valves, isolated aortic root aneurysms, ascending aorta, and root aneurysms) can be useful during the development of TARR technologies, before performing animal experiments.

Study Limitations

Limitations of this study are small number of tested aortic roots, limits of the available 3D-printing technology that cannot yet easily reproduce small details, nonpulsatile hydrodynamic model for coronary tests, use of water, and absence of coronary resistances.

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